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David C. Foster Suite 3400 Four Embarcadero Center San Francisco, CA 94111-4187			EXAMINER WHISENANT, ETHAN C	
			ART UNIT	PAPER NUMBER
			1634	
DATE MAILED: 02/26/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

*S.A.M.*

## Office Action Summary

**Application No.**

10/045,575

**Applicant(s)**

GUNDERSON ET AL.

**Examiner**

Ethan Whisenant, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 October 2002 and 30 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 15-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **NON-FINAL ACTION**

- 1.** The applicant's Preliminary Amendments filed 03 OCT 02 and 30 JUN 03 have been entered. Following the entry of the Preliminary Amendments, **Claim(s) 15-37** is/are pending.

### **PRIORITY**

- 2.** An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Please note that the applicant in their IDS state that they are relying on USSN 09/553,993 filed 20 APR 00 and USSN 09/556,463 filed 21 APR 00 for priority. The examiner notes that other papers in the application (i.e. the declaration and the first paragraph of the specification) indicate that the applicant is claiming priority only to US provisional application 60/244,119 filed 26 OCT 00. Please clarify the priority claim and update the first paragraph of the specification as necessary.

### **35 USC § 112- 2ND PARAGRAPH**

- 3.** The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

### **CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH**

- 4.** **Claim(s) 15-26** is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**Claim 15** is indefinite because there is no nexus between the preamble and the claim steps. Claim 15 in its preamble directs to a method which is to accomplish a particular goal. However, none of the claim steps states that this goal is accomplished. For clarity, claimed methods should recite

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that the purpose of the method has been attained (i.e. provide a nexus between the preamble and the claim steps).

**Claim 20** is indefinite because part ii of step f) is nonsequitur. The phrase that appears to make this step confusing is "comprising at least a first subpopulation comprising". Please clarify at least part ii of step f).

**Claim 26** is indefinite because it is unclear as to what "comprising at least a first subpopulation comprising" refers. Please clarify.

### 35 USC § 102

**5.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

**6.** The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

**Claim Rejections under 35 USC § 102**

**7.** Claim(s) 15-19, 27, and 34-37 is/are rejected under 35 U.S.C. 102(b) as being anticipated by Nikiforov et al. [US 5,679,524 (1997)].

**Claim 15** is drawn to a method of genotyping an allele of a target nucleic acid sequence which method comprises five required steps. To begin, a target nucleic acid sequence comprising a first domain and a second domain, wherein said first and said second domains are separated by a detection position is provided, Next, a first hybridization complex is formed by hybridizing a first primer comprising an adapter sequence to said first domain immediately adjacent to and 3' of said detection position and hybridizing a second primer to said second domain, immediately adjacent to and 5' of said detection position Then, the first hybridization complex is contacted with dNTPs and a first enzyme to form a modified hybridization complex. Next, the modified hybridization complex is contacted with a second enzyme to form a ligated probe. Finally, the presence of said ligated probe is detected.

**Claim 16** is drawn to an embodiment of Claim 15 wherein said first enzyme is a polymerase. **Claim 17** is drawn to an embodiment of Claim 15 wherein second enzyme is a ligase. **Claim 18** is drawn to an embodiment of Claim 15 wherein the dNTPs comprise a label. **Claim 19** is drawn to an embodiment of Claim 18 wherein the label is a fluorescent label.

Nikiforov et al. teach a method comprising all of the limitations recited in Claim 15-19 and 27. See at least, for example, Col. 6 - Col. 16, note also Figure 4. As regards the limitation in Claim 15 "a primer comprising an adapter sequence", Note that the molecule in Fig. 4, No. 2. and No. 3. comprise an adapter sequence (i.e. that part of the linker sequence not hybridized to template and attached at its 3' end to FITC). Also note that Nikiforov et al. teach many different embodiments of their invention including one where the primer sequence is the oligo comprising a nucleic acid sequence that is not complementary to the target nucleic acid (i.e. the adapter sequence) and is attached to a FITC molecule and the linker sequence is the ligated oligo. Essentially, the reverse of Figure 4, panel 1.

**35 USC § 103**

**8.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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**9.** This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

#### **CLAIM REJECTIONS UNDER 35 USC § 103**

**10.** Claim(s) 20-24 and 28-33 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov et al. [US 5,679,524 (1997)] as applied above and further in view of Walt et al. [US 6,327,410 (2001)].

**Claim 20** is drawn to an embodiment of Claim 15 wherein the ligated probe comprising said adapter sequence is contacted with an array comprising a substrate with a surface comprising discrete sites and a population of microspheres distributed on said surface which microspheres comprise at least one first capture probe, such that said first capture probe and said ligated probe form a second hybridization complex; and finally detecting the presence of said second hybridization complex.

Nikiforov et al. teach detecting their ligated probe via hybridization and capture onto a solid support. See especially Col. 12, lines 11-14 which states "Hybridization, extension and ligation may also be performed in solution and the ligated oligonucleotides captured onto a solid phase for detection (FIG. 4)." In addition, in Col. 11, beginning at about line 6, Nikiforov et al. teach the solid supports that may be used to practice their method. Nikiforov et al. teach "The solid support can be glass, plastic, paper, etc. The support can be fashioned as a bead, dipstick, test tube, or a variety of other shapes.

In view of these teachings, it can be said that Nikiforov et al. teach all of the limitations recited in Claim 20 except these authors do not explicitly teach using a population of microspheres comprising at least one first capture probe which microspheres are distributed on the surface of a substrate. However, Walt et al. do teach compositions, as well as methods utilizing these compositions, which compositions comprise a substrate with a surface comprising discrete sites, and a population of microspheres (i.e. beads) - with probes attached thereto - distributed on the sites.

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Absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Nikiforov et al. wherein the detection step is performed using the composition/method taught by Walt et al.

Please note that substitution of one well known method/reagent with well known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

**Claim 21** is drawn to an embodiment of Claim 20 wherein said substrate is a fiber optic bundle. **Claim 22** is drawn to an embodiment of Claim 20 wherein said substrate is selected from a defined group which includes glass and plastic. **Claim 23** is drawn to an embodiment of Claim 15 wherein said discrete sites comprise wells. **Claim 25** is drawn to an embodiment of Claim 15 wherein the method further comprises contacting the ligated probe with an ordered array, wherein said ordered array comprises capture probes. **Claim 26** is drawn to an embodiment of Claim 15 wherein the method further comprises contacting the ligated probe with a population of microspheres comprising at least a first capture probe, such that said first capture probe and said ligated probe comprising said adapter sequence form a second hybridization complex.

Walt et al. teach the limitations of Claims 21-22, see at least for example, Col. 5 about lines 32 - 48, wherein these authors teach "The compositions comprise a substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon.TM., etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, optical fiber bundles, and a variety of other polymers. In general, the substrates allow optical detection and do not appreciably fluoresce. As regards Claim 23 see, at least for example, Col. 4, lines 9-12 of Walt et al. As regards Claims 25-26 see, at least for example, Col. 10, at about line 43 - Col. 11, line 22 of Walt et al.

**Claim 24** is drawn to an embodiment of Claim 15 wherein said second primer further comprises an adapter sequence.

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Neither, Nikiforov et al. or Walt et al. explicitly teach a an embodiment wherein both the ligation probe and the primer comprise adapter sequences. Nikiforov et al. do teach that either the primer or the ligation probe may comprise the adapter sequence (i.e. a nucleic acid sequence which is not complementary to target but which is complementary to a capture probe. Therefore, as the use of adapter sequences was well known in the art at the time of the invention, the attachment of a second adapter sequence to the second primer of Nikiforov et al. would have been, absent an unexpected result, *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Please note that substitution of one well known method/reagent with well known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09. Furthermore, in view of the teachings in Nikiforov et al. and Walt et al. it would have been *prima facie* obvious to the ordinary artisan at the time of the invention to add a second adapter sequence to the ligation product (i.e. to the primer) of Nikiforov et al. because the addition of a second adapter would increase the speed with which hybridization would occur at the time of detection.

As regards **Claims 28-33** see the explanation above for Claims 20-26 which recite essentially the same embodiments of the invention.




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**CONCLUSION**

**11.** Claim(s) 1-37 is/are rejected and/or objected to for the reason(s) set forth above.

**12.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

The fax number for this Examiner is (571) 273-0754. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

  
**ETHAN WHISENANT**  
**PRIMARY EXAMINER**

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